REPORTS OF PRACTICAL ONCOLOGY AND RADIOTHERAPY 18 (2013) S386–S390

SciVerse ScienceDirect

journal homepage: http://www.elsevier.com/locate/rpor

Translational research in cancer

Cancer stem cell in larynx carcinoma: Resistance or sensibility?

M. Martín[1], C. Gamallo[2], M. Guijarro[2], M. Lopez[1], O. Leaman[1], O. Liñan[1], L. Cerezo[1]

[1] *Hospital Universitario De La Princesa, Oncología Radioterápica, Spain*

[2] *Hospital Universitario De La Princesa, Anatomía Patológica, Spain*

Introduction. Cancer may arise from mutations in stem cell populations. According with this theory, only a specific subpopulation of cancer cells have the ability to sustain cancer growth, and are resistant to chemo and radiotherapy. These cells are called cancer stem cells (CSC). The aldehyde dehydrogenase (ALDH1) a marker for CSC, is a cytosolic isoenzyme responsible for oxidizing intracellular aldehehydes and contributing to the oxidation of retinol to renoic acid in early stem cell differentiation. Furthermore, activity of the ALDH1 enzyme has been identified as being responsible for the resistance to chemotherapeutic agents and radiotherapy.

Objetive. We analysed the ALDH1 expression in epidermoid laryngeal carcinoma treated with radiotherapy o radiochemotherapy in attempt to evaluate the role of such a cancer population in the efficacy of radiotherapy.

Methods. The expression of ALDH1A1 was studied in 25 pts treated in our department from January 2006 to December 2011 for larynx carcinoma. A standard immunohistochemical technique for ALDH1A1 was used. The results were correlated with the site of the tumor, stage and prognosis.

Results. 32% of tumors were positive for ALDH1A1. With a median of 35 months of follow up, no differences were founded for the whole group for relapse-free (RFS) or overall survival (OS). When stage I was excluded from the analysis, better RFS was linked with expression of ALDH1 (83.3 vs. 16.9 p: 0.015). In multivariate analysis stage (II–III vs. IV HR 0.055 p: 0.02) and ALDH1 expression (negative vs. positive HR 21.5 p: 0.02), maintained independent prognostic relevance.

Conclusions. Our findings suggest that ALDH1 expression, a CSC marker, is associated with favourable prognosis and better response to radiotherapy. It may be that not all CSC are resistant to radiation or that ALDH1 is not a suitable CSC marker because terminally differentiated cancer cells can preserve its expression.

http://dx.doi.org/10.1016/j.rpor.2013.03.634

Carnosic acid: Radioprotective effects against damage induced by ionizing radiation

A. Olivares, D. Achel, M. Alcaraz, E. Olmos, M. Alcaraz-saura, J. Castillo

Faculty of Medicine/Dentistry, University of Murcia, Radiology and Physical Medicine, Murcia, Spain

Purpose. To determine the genoprotective and radioprotective capacity of carnosic acid (CAR) in non-tumour cells (lymphocytes and prostate epithelial cells) against damage induced by ionizing radiation with similar effects produced by different antioxidant compounds.

Methods. The genoprotective effect was studied by means of the micronucleus assay for antimutagenic activity in which the reduction in the frequency of micronuclei was evaluated in cytokinesis-blocked cells of human lymphocytes; a method described by Fenech and Morley (1985) and adapted by the International Atomic Energy Agency (2011). To analyze the radioprotective effects of the substances studied on cell viability and survival, we used the MTT assay for 24 or 48 h in PNT2 cell lines when they were administered before and after exposure to different X-ray doses (4, 6, 8, 10 and 0 Gy).

Results. CAR led to a significant drop in the frequency of MN which expresses the significant genoprotective capacity ($p < 0.001$) against X-ray induced chromosome damage with a protection factor of 50%, and a dose reduction factor of 4.3. Cell survival obtained with the substance showed an increase at the highest dose used, which is an expression of radioprotective capabilities,

1507-1367/$ – see front matter

showing the highest protection factor of 55.1%, and eliminating 39% of radiation induced cell death in cells PNT2 ($p < 0.001$). The results point to a significant genoprotective capacity of the different substances assayed with a maximum radiation protection factor of 60% and a dose-reduction factor of 4.9 for CAR. Cell survival obtained with CAR administered with up to 10 Gy showed a Protection Factor of 100%, eliminating 30.8% of radioinduced cell death.
Conclusions. In the normal epithelial cells CAR acts as an antioxidant which can eliminate the excess free radicals induced by IR in conjunction with the intracellular redox defensive system. Acknowledgments This report was supported by a grant from the Seneca Foundation and other grant from Programme CENIT denominated SENIFOOD.

http://dx.doi.org/10.1016/j.rpor.2013.03.635

Controversies in the association between radiation toxicity and TGF-BETA1 polymorphisms

J. Lopez Guerra[1], E. Montero[1], I. Rincon[1], M. Carrasaco[2], M. Baeza[2], R. Peñalver[1], J. Praena Fernandez[3], D. Gomez[4], Z. Liao[4], M. Ortiz[1]
[1] *Hospitales Universitarios Virgen Del Rocío, Radiation Oncology, Spain*
[2] *Hospitales Universitarios Virgen Del Rocío, Radiation Physics, Spain*
[3] *Hospitales Universitarios Virgen Del Rocío, Methodology Unit, Fundación Pública Andaluza para la Gestión de la Investigación en Salud de Sevilla, Spain*
[4] *The University of Texas MD Anderson Cancer Center, Radiation Oncology, Spain*

Background. Several groups have studied the association between TGF-b1 single nucleotide polymorphisms (SNPs) and the risk of developing radiation-induced lung toxicity (RILT) in patients with lung cancer.
Aim. The objective of this study was to carefully assess the potential reasons for the contradictory results reported about this topic.
Methods. A search was based on PubMed electronic database. The following terms and limits were explored and used for the database search: TGF, lung cancer, polymorphisms, and radiation. We then assessed potential confusing factors including the ethnicity, endpoint used, and the analysis methodology that may explain the difference in findings among the reports.
Results. Three studies (U.S., European, and Chinese) were found using the terms and limits mentioned above. The Chinese and European studies could not validate the previously association found in a US cohort between the CT/CC genotypes of SNP rs1800470 and a lower risk for treatment related pneumonitis. Several potential reasons that may explain this divergence were found. First, there were differences in the distribution of allele frequencies and genotypes among the three analyzed cohorts ($P < 0.001$). Second, in the European study lung toxicity was scored using the CTC v3.0 for dyspnea. In contrast, the U.S. and Chinese studies assessed the development of RILT including radiologic findings for changes in the lung. Finally, whereas the U.S. and Chinese studies included the event time into account in their analyses, the European study did not consider it in the RILT calculation.
Conclusions. Our findings suggest that the frequency patterns of polymorphisms in TGF-b1 gene vary greatly among different ethnic groups. In addition, it is expected that the results would be different if the studies being compared are studying different endpoints and using different statistical analysis methodology. A prospective validation is needed to elucidate the association between RILT and TGF SNPs.

http://dx.doi.org/10.1016/j.rpor.2013.03.636

Effects of radiation on human mesenchymal stem cells

L. Glaria Enríquez[1], C. Huerga Cabrerizo[2], D. García Olmo[3], M. García Arranz[4], C. Largo[5]
[1] *Hospital Universitario La Paz, Oncología Radioterá'pica, Spain*
[2] *Hospital Universitario La Paz, Radiofísica y Radioprotección, Spain*
[3] *Hospital Universitario La Paz, Cirugía General, Spain*
[4] *Hospital Universitario La Paz, Unidad de Terapia Celular, Spain*
[5] *Hospital Universitario La Paz, Cirugía Experimental, Spain*

Introduction. A growing number of studies have shown that a small proportion of tumor stem cells (TSC) exists in the tumor cell population. The TSC has a powerful capacity for self-renewal and tumor initiation. They are resistant to chemotherapy and radiotherapy. Moreover stem cells of normal tissues (NTSC) are important in the repair and recovery after damage induced by radiation.
Objective. To find it's radiation response profile we performed irradiation experiments on mesenchymal cells derived from human adipose tissue characterized by international standards.
Methods. We compared two different irradiation sources of linear energy transfer (LET): 6 MV photons from linear accelerator and radiation sources I125. Was studied a dose range of 0.5–2 Gy. Original design was conducted in which, using a limited number of sources and cells can be efficiently establish a curve of dose response and mortality analyze and cell proliferation.